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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Sep 17	IMSworld Pharmaceutical Company Directory name change to PHARMASEARCH
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NEWS 4	Oct 09	Number of Derwent World Patents Index updates increased
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NEWS 6	Oct 22	Over 1 million reactions added to CASREACT
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NEWS 9	Nov 19	New Search Capabilities USPATFULL and USPAT2
NEWS 10	Nov 19	TOXCENTER(SM) - new toxicology file now available on STN
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NEWS 13	Nov 30	Files VETU and VETB to have open access
NEWS 14	Dec 10	WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS 15	Dec 10	DGENE BLAST Homology Search
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NEWS 19	Dec 19	CAS Roles modified
NEWS 20	Dec 19	1907-1946 data and page images added to CA and CAplus
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L5 ANSWER 1 OF 12 MEDLINE DUPLICATE 1
2001392843 Document Number: 21340434. PubMed ID: 11447389. Roles of carbohydrates on **Cry j 1**, the major allergen of **Japanese cedar pollen**, in specific T-cell responses. Okano M; Kino K; Takishita T; Hattori H; Ogawa T; Yoshino T; Yokoyama M; Nishizaki K. (Departments of Otolaryngology and Pathology, Okayama University Medical School, Okayama, Japan.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (2001 Jul) 108 (1) 101-8. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: Carbohydrates expressed on allergens are known to be important for allergenicity. However, little is known about whether the carbohydrates drive the T(H)2 response. OBJECTIVE: We sought to determine a role for carbohydrates expressed on **Cry j 1**, which is the major allergen of Cryptomeria japonica pollen and causes the most prevalent pollinosis in Japan, in in vitro cellular responses. METHODS: Carbohydrates on **Cry j 1** were destroyed by periodate-oxidation under mild conditions. Proliferative responses and cytokine productions against native, periodate-treated, and mock-treated **Cry j 1** were compared in peripheral blood mononuclear cells, **Cry j 1**-specific T-cell lines, and clones from patients with Japanese cedar pollinosis. RESULTS: We found that peripheral blood mononuclear cells from patients with Japanese cedar pollinosis displayed a significant decrease

in proliferation and IL-5 production in response to periodate-treated **Cry j 1** in comparison with native and mock-treated **Cry j 1**. Decreased proliferative responses against periodate-treated **Cry j 1** were also seen in polyclonal T-cell lines, and the responses showed a heterogeneity. In addition, **Cry j 1** -specific CD4+ T-cell clones also displayed a significant decrease in proliferation and IL-4 and IL-5 production-but not IFN-gamma production-in comparison with the control antigens. However, most of the clones showed decreased but positive proliferative responses against periodate-treated **Cry j 1**. Blockade of the mannose receptor had no effect on cellular responses. CONCLUSION: The results suggest that carbohydrates on **Cry j 1** play a major role in promoting **Cry j 1**-specific T(H)2 response in vitro, though they are not major targets as **T-cell epitopes**.

L5 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2002 ACS

2000:303759 Document No. 133:72863 Common antigenicity between Japanese cedar (Cryptomeria japonica) pollen and Japanese cypress (Chamaecyparis obtusa) pollen, II. Determination of the cross-reacting **T-cell epitope** of **Cry j 1** and Cha o 1 in mice. Ohno, N.; Ide, T.; Sakaguchi, M.; Inouye, S.; Saito, S. (Department of Pediatrics, Department of Molecular Immunology, Institute of DNA Medicine, The Jikei University School of Medicine, Tokyo, 105-8461, Japan). Immunology, 99(4), 630-634 (English) 2000. CODEN: IMMUAM. ISSN: 0019-2805. Publisher: Blackwell Science Ltd..

AB We have previously detected common antigenicity between **Cry j 1** and Cha o 1 in B10.S mice. B10.S mice immunized with **Cry j 1**- or Cha o 1-generated T cells and antibodies reactive to both allergens. In the present study, we investigated the cross-reacting and **Cry j 1** -specific **T-cell epitopes** in B10.S mice. Lymph node cells from B10.S mice immunized with **Cry j 1** recognized **Cry j 1** p111-130, p211-230, and p310-330 as well as Cha o 1 p209-228. The existence of the cross-reacting **T-cell epitope** in **Cry j 1** and Cha o 1 was confirmed by the response of newly established p211-230-specific and Cha o 1 p209-228-specific T-cell lines. The min. peptide sequence (p213-224) of the cross-reacting **T-cell epitope** was identical in **Cry j 1** and Cha o 1. These findings clearly demonstrate that common antigenicity at the T-cell level between Japanese cedar and cypress pollen allergens was caused by the existence of an identical-cell epitope in **Cry j 1** and Cha o 1.

L5 ANSWER 3 OF 12 MEDLINE DUPLICATE 2

2000253159 Document Number: 20253159. PubMed ID: 10792511. Common antigenicity between Japanese cedar (Cryptomeria japonica) pollen and Japanese cypress (Chamaecyparis obtusa) pollen, I. H-2 complex affects cross responsiveness to **Cry j 1** and Cha o 1 at the T- and B-cell level in mice. Kingetsu I; Ohno N; Hayashi N; Sakaguchi M; Inouye S; Saito S. (Department of Internal Medicine (III), Institute of DNA Medicine, The Jikei University School of Medicine, Tokyo, Japan.) IMMUNOLOGY, (2000 Apr) 99 (4) 625-9. Journal code: GH7; 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Common antigenicity among two purified **Japanese cedar pollen** allergens (**Cry j 1** and Cry j 2) and one Japanese cypress pollen allergen (Cha o 1) was explored at the T-cell and B-cell level in mice of different H-2 haplotypes. Cry j 2 did not show any common antigenicity with **Cry j 1** or Cha o 1. B10.S (H-2S) mice immunized with **Cry j 1** or Cha o 1 generated T cells and antibodies reactive to both antigens, indicating the common antigenicity of these antigens. C57BL/6 (H-2b) mice were non-responders to **Cry j 1**.

BALB/c (H-2d) mice immunized with **Cry j 1** or Cha o 1 and C57BL/6 mice immunized with Cha o 1 generated T cells that were only reactive with the respective immunogen, but produced antibody reactive to both **Cry j 1** and Cha o 1, indicating that **Cry j 1** and Cha o 1 share their B-cell epitope but not their **T-cell epitope**. This finding may provide a clue for the clarification of the T-cell and B-cell epitopes of **Cry j 1** and Cha o 1, even though the data are influenced by H-2 complex restriction in mice. Considering that H-2 complex restriction affects cross responsiveness to **Cry j 1** and Cha o 1 at the T- and B-cell level in mice, we assessed the possible situation in humans exposed sequentially to **Japanese cedar pollen** and Japanese cypress pollen.

L5 ANSWER 4 OF 12 MEDLINE DUPLICATE 3

2000157072 Document Number: 20157072. PubMed ID: 10692034. Inhibition of immunoglobulin E response to **Japanese cedar pollen** allergen (**Cry j 1**) in mice by DNA immunization: different outcomes dependent on the plasmid DNA inoculation method. Toda M; Sato H; Takebe Y; Taniguchi Y; Saito S; Inouye S; Takemori T; Sakaguchi M. (Department of Immunology, AIDS Research Center and Infectious Disease Surveillance Center, National Institute of Infectious Diseases, Tokyo, Japan.) IMMUNOLOGY, (2000 Feb) 99 (2) 179-86. Journal code: GH7; 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB To develop a new immunotherapy for Japanese cedar (Cryptomeria japonica; CJ) pollinosis, we evaluated the use of DNA immunization by inoculating mice with plasmid DNA encoding **Cry j 1** as a CJ pollen major allergen (pCACJ1). Repeated intramuscular (i.m.) inoculation of BALB/c mice with pCACJ1 produced anti-**Cry j 1** antibody responses, which were predominately of the immunoglobulin G2a (IgG2a) type. Furthermore, this inoculation suppressed immunoglobulin E (IgE) and IgG1 antibody responses to subsequent alum-precipitated **Cry j 1** injections. Splenic T cells isolated from mice inoculated with pCACJ1 i.m. secreted interferon-gamma (IFN-gamma), but not interleukin (IL)-4, in vitro upon stimulation with **Cry j 1** as well as with p277-288, a peptide corresponding to the **T-cell epitope** of **Cry j 1**. In contrast, inoculation of BALB/c mice with pCACJ1 by gene gun injection caused response predominantly of the IgG1 type, and enhanced production of anti-**Cry j 1** IgE antibodies to subsequent alum-precipitated **Cry j 1** injections. Splenic T cells isolated from pCACJ1-innoculated mice by gene gun injection secreted both IFN-gamma and IL-4 in vitro, upon stimulation with **Cry j 1** as well as with p277-288. These findings suggest that i.m. inoculation with pCACJ1 effectively elicits **Cry j 1**-specific T helper 1 (Th1)-type immune responses, resulting in inhibition of the IgE response to **Cry j 1**.

L5 ANSWER 5 OF 12 MEDLINE DUPLICATE 4

1999367828 Document Number: 99367828. PubMed ID: 10436390. Peptide specificity, HLA class II restriction, and T-cell subsets of the T-cell clones specific to either **Cry j 1** or Cry j 2, the major allergens of Japanese cedar (Cryptomeria japonica) pollen. Sone T; Morikubo K; Shimizu K; Komiyama N; Tsunoo H; Kino K. (Department of Pharmaceutical Research, Meiji Institute of Health Science, Kanagawa, Japan.. sonetosi@saitama-med.ac.jp) . INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1999 Jul) 119 (3) 185-96. Journal code: BJ7; 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: **Cry j 1** and Cry j 2 are thought to be the major allergens of **Japanese cedar pollen**. HLA class II types capable of presenting **T-**

cell epitopes in both allergens and their role in induction of T-cell subsets are not well known. METHODS: CD4+ T (Th)-cell clones (TCCs) specific to either **Cry j 1** or Cry j 2 were generated. HLA class II restrictions were determined by their reactivity to the **T-cell epitope** in the presence of antigen presenting cells sharing matched types. Interleukin (IL)-2, interferon-gamma, IL-4, and IL-5 contents in the supernatants of TCCs were estimated using enzyme immunoassay. RESULTS: Peripheral blood mononuclear cells (PBMC) from patients induced proliferation with 100 microgram/ml **Cry j 1** or 3-10 microgram/ml rCry j 2 stimulation. **T-cell epitopes** in **Cry j 1** were presented to Th cells by the gene products of DRA1*01/DRB1*0901, DRA1*01/DRB5*0101, DQA1* 0102/DQB1*0602, and DPA1*01/DPB1*0501; those in Cry j 2 were restricted by DRA1*01/DRB1*0901, DRA1* 01/DRB1*1501, DRA1*01/DRB4*01, DRA1*01/DRB5* 0101, DQA1*0102/DQB1*0602, DPA1*01/DPB1*0201, and DPA1*01 and *0202/DPB1*0501. Type 2-like cells were preferentially induced in **Cry j 1** stimulation, while an almost equal number of type 2- and type 1-like cells was induced in rCry j 2. CONCLUSIONS: No clear correlation existed between peptide specificity, HLA class II restriction and induction of Th-cell subsets, suggesting that the requirement of different dose of **Cry j 1** or Cry j 2 to induce proliferation in PBMC may lead to distinguishable difference in induction of Th subsets between TCCs specific to **Cry j 1** and Cry j 2.

L5 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS
1998:338149 Document No. 129:27001 Peptide immunotherapeutic agent. Sone, Toshio; Kume, Akinori; Dairiki, Kazuo; Kino, Kohsuke (Meiji Milk Products Co., Ltd., Japan; Sone, Toshio; Kume, Akinori; Dairiki, Kazuo; Kino, Kohsuke). PCT Int. Appl. WO 9820902 A1 19980522, 51 pp. DESIGNATED STATES: W: AU, CA, CN, JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1997-JP4129 19971112. PRIORITY: JP 1996-302053 19961113.
AB A peptide immunotherapeutic agent useful for each individual patient suffering from an allergy, and a reagent for a typing test on HLA class II mols. of the patient to be used in the selection of a peptide immunotherapeutic agent useful for each individual patient suffering from an allergy. The peptide immunotherapeutic agent permits the optimal peptide immunotherapy for each individual patient, so that a marked improvement in peptide immunotherapy can be expected. Further, it has become possible to provide a peptide immunotherapeutic agent which is useful also for patients who cannot be covered by peptide immunotherapy by a major antigen peptide recognized in a particular patient population. Furthermore, it has also become possible to conveniently conduct typing of HLA class II mols. of patients suffering from an allergy by using the antigen peptide of the invention. Thus, **T cell epitopes** of **Japanese cedar pollen** allergen Cry i 1 and 2 were identified for immunotherapy of allergy.

L5 ANSWER 7 OF 12 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 5
1998409877 EMBASE Identical recognition of **T-cell epitopes** by Th1 and Th2 subsets in mice immunized with **Japanese cedar pollen** antigens. Kingetsu I.; Saito S.. I. Kingetsu, Dept. of Internal Medicine (III), 3-25-8, Nishi-Shinbashi, Minato-ku, Tokyo 105-8461, Japan. Jikeikai Medical Journal 45/3 (95-105) 1998.
Refs: 24.
ISSN: 0021-6968. CODEN: JMEJAS. Pub. Country: Japan. Language: English. Summary Language: English.
AB To investigate the **T-cell epitopes** of antigen involved in preferential expansion of helper T cell type 1 (Th1) and type 2 (Th2) subsets in vivo, three mouse strains were immunized with **Cry j 1** or Cry j 2, major allergens of **Japanese cedar pollen**, in different adjuvant

formulations. Immunization with the antigen in aluminium hydroxide induced a strong Th2 response, characterized by the production of IL-4 and IL-10, in BALB/c and B10.S mice but induced a weak Th2 response in C57BL/6 mice. In contrast, when complete Freund's adjuvant was used. Th1 response, characterized by interferon-.gamma. production, was strongly induced in C57BL/6 and B10.S mice but weakly induced in BALB/c mice. These results suggest that the polarization of Th1 or Th2 responses against the same antigen was strongly affected by the adjuvant employed. We next explored the **T-cell epitopes** on the antigen recognized by each Th subset using overlapping peptides spanning the entire sequence of each allergen. Although four major determinant regions (p 78-91, p 246-259, p 318-331, p 370-383) on Cry j 2 were observed in C57BL/6 mice, there was no difference among **T-cell epitopes** recognized by both T-cell subsets. In addition, in BALB/c mice immunized with **Cry j 1** in different adjuvants formulations, both T-cell subsets recognized the same T-cell determinant (p 271-190). These results suggest that Th1 and Th2 cells induced in vivo against the same antigen cannot distinguish **T-cell epitopes**.

L5 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS
1997:428733 Document No. 127:107629 T cell responsiveness to allergen. Ikagawa, Shuji; Ishikawa, Takeru (Igakubu, Kumamoto Daigaku, Kumamoto, 860, Japan). Arerugi no Ryoiki, 4(7), 930-935 (Japanese) 1997. CODEN: ARRYFB. ISSN: 1340-2358. Publisher: Iyaku Janarusha.
AB A review with 11 refs. on antigen presentation to T cells, on cytokine prodn. patterns of antigen-specific T cells, on analyses of **T cell epitopes** of major allergens, and on T cell responses to **Japanese cedar pollen** allergen (**Cry j 1**).

L5 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS
1997:282895 Document No. 126:342174 Human T cell response to antigen peptides of **Japanese cedar pollen** (**Cry j 1**). Ishikawa, Takeru; Ikagawa, Shuji; Masuyama, Keisuke; Matsushita, Sho; Nishimura, Yasuharu (Department of Otorhinolaryngology, Kumamoto University School of Medicine, Kumamoto, 860, Japan). Int. Arch. Allergy Immunol., 113(1-3), 255-257 (English) 1997. CODEN: IAAIEG. ISSN: 1018-2438. Publisher: Karger.
AB The aim of this study was to det. the peptide epitope reactivity of T cells from patients allergic to **Japanese cedar pollen** (Cryptomeria japonica) and to discuss whether immunotherapy could control T cell response to the allergen, which is the fundamental and essential way of controlling IgE antibody prodn.

L5 ANSWER 10 OF 12 MEDLINE
96406689 Document Number: 96406689. PubMed ID: 8810803. Molecular immunology of **Japanese cedar pollen** allergens: analysis of **T cell epitopes**. Hashiguchi S; Sugimura K. (Department of Molecular Biology, Faculty of Engineering, Kagoshima University.) NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (1996 Aug) 54 (8) 2233-42. Ref: 24. Journal code: KIM; 0420546. ISSN: 0047-1852. Pub. country: Japan. Language: Japanese.
AB Recent studies demonstrated that partial alteration of the amino acid sequence of **T cell epitopes** induced a stimulatory signal that was qualitatively different. Therefore, it is conceivable that immunotherapy using peptides representing dominant **T cell epitopes** could modulate the T cell response of allergic patients and prevent the production of IgE antibodies. Accordingly, a number of allergens have been molecularly cloned to determine their amino acid sequences. In Japan, the number of patients suffering from Japanese cedar pollinosis is steadily increasing and it has become a serious social problem. In this paper, we review the recent advances on **T cell epitope** mapping of **Japanese cedar pollen**, **Cry j**

1 and Cry j 2 and immunomodulating trials based on the mechanisms of T cell antigen-recognition.

L5 ANSWER 11 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 6

1996:358924 Document No.: PREV199699081280. Japanese cedar pollinosis and HLA-DP5. Hori, T.; Kamikawaji, N.; Kimura, A.; Sone, T.; Komiyama, N.; Komiyama, S.; Sasazuki, T. (1). (1) Dep. Genet., Med. Inst. Bioregulation, Kyushu Univ., 3-1-1 Maidashi, Higashi-ku, Fukuoka 812 Japan. Tissue Antigens, (1996) Vol. 47, No. 6, pp. 485-491. ISSN: 0001-2815. Language: English.

AB Japanese cedar pollinosis is a type I allergic disease caused by Japanese cedar (Cryptomeria japonica) pollen. We investigated the association between the disease and HLA class II alleles by HLA-DNA typing using a PCR-SSOP method and found that the frequency of HLA-DP5 (DPA1*02022 and DPB1*0501) was significantly increased in the patients. To investigate whether the HLA-DP5 molecule is directly involved in the pathogenesis of the disease, **Japanese cedar pollen** antigen (CPAg)-specific T cell lines were established from 3 patients who possessed HLA-DP5 (DPA1*02022/ DPB1*0501). By using these CPAg-specific T cell lines and HLA class II-expressing L-cell transfectants, we found that disease-associated HLA-DP5 restricted T cells specific for CPAg existed in the patients. Furthermore, among 38 synthesized overlapping peptides spanning the entire length of one of the major **Japanese cedar pollen** allergens, **Cry j 1**, an immunodominant peptide which induced HLA-DP5 restricted Th2 was identified. These observations suggest that the HLA-DP5 may be involved, at least in part, in the pathogenesis, by helping the IgE antibody production against CPAg.

L5 ANSWER 12 OF 12 MEDLINE DUPLICATE 7

96152251 Document Number: 96152251. PubMed ID: 8568138. Single amino acid substitutions on a **Japanese cedar pollen** allergen (**Cry j 1**)-derived peptide induced alterations in human T cell responses and T cell receptor antagonism. Ikagawa S; Matsushita S; Chen Y Z; Ishikawa T; Nishimura Y. (Department of Neuroscience and Immunology, Kumamoto University Graduate School of Medical Sciences, Japan.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1996 Jan) 97 (1 Pt 1) 53-64. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB We generated T cell clones specific to a **Japanese cedar pollen** allergen (**Cry j 1**) and investigated effects of altered T cell receptor (TCR) ligand on changes of T cell responses. One of these **Cry j 1**-specific T cell clones established from patients with Japanese cedar pollinosis, ST1.9, recognized an antigenic peptide **Cry j 1** p335-346 in the context of HLA-DRA+DRB3*0301 molecules and secreted interleukin-4 dominantly, with a smaller amount of interferon-gamma. ST1.9 represented one of the major T cell clones specific to **Cry j 1** in the donor, because a short-term cultured polyclonal T cell line specific to **Cry j 1** exhibited the same character as the ST1.9. We synthesized various analog peptides derived from **Cry j 1** p335-346 with single amino acid substitutions and determined key residues for interactions between TCR of ST1.9 and HLA-DR molecules. We also analyzed changes in the responses of ST1.9 to **Cry j 1** p335-346-derived analog peptides. Of interest was that the substitution of 339threonine to valine resulted in a significant increase in interferon-gamma production, with no remarkable changes either in proliferative response or interleukin-4 production. Analog peptides carrying the substitutions of 339threonine to glycine or glutamine revealed TCR antagonism, without changes in their binding affinities to the DR molecule. Therefore single amino acid substitutions on an allergen peptide carrying the **T cell epitope** may suppress helper-T-dependent class switch pressure to IgE in B cells either

by inducing increased interferon-gamma production or by inhibiting proliferative responses in helper-T cells.

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L2 707 S JAPANESE CEDAR POLLEN
L3 113 S L2 AND "CRY J 1"
L4 35 S L3 AND T CELL EPITOPE
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L7 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1999:371144 Document No.: PREV199900371144. Peptide specificity, HLA class II restriction, and T-cell subsets of the T-cell clones specific to either Cry j 1 or Cry j 2, the major allergens of Japanese cedar (Cryptomeria japonica) pollen. Sone, Toshio (1); Morikubo, Keiko; Shimizu, Kimiko; Komiyama, Naoki; Tsunoo, Hajime; Kino, Kohsuke. (1) Department of Medical Zoology, Saitama Medical School, 38 Morohongo, Moroyama, Iruma, Saitama, 350-0495 Japan. International Archives of Allergy and Immunology, (July, 1999) Vol. 119, No. 3, pp. 185-196. ISSN: 1018-2438. Language: English. Summary Language: English.

AB Background: Cry j 1 and Cry j 2 are thought to be the major allergens of **Japanese cedar pollen**. HLA class II types capable of presenting T-cell epitopes in both allergens and their role in induction of T-cell subsets are not well known. Methods: CD4+ T (Th)-cell clones (TCCs) specific to either Cry j 1 or Cry j 2 were generated. HLA class II restrictions were determined by their reactivity to the T-cell epitope in the presence of antigen presenting cells sharing matched types. Interleukin (IL)-2, interferon-gamma, IL-4, and IL-5 contents in the supernatants of TCCs were estimated using enzyme immunoassay. Results: Peripheral blood mononuclear cells (PBMC) from patients induced proliferation with 100 mug/ml Cry j 1 or 3-10 mug/ml rCry j 2 stimulation. T-cell epitopes in Cry j 1 were presented to Th cells by the gene products of DRA1*01/DRB1*0901, DRA1*01/DRB5*0101, DQA1* 0102/DQB1*0602, and DPA1*01/DPB1*0501; those in Cry j 2 were restricted by DRA1*01/DRB1*0901, DRA1*01/DRB1*1501, DRA1*01/DRB4*01, DRA1*01/DRB5* 0101, DQA1*0102/DQB1*0602, DPA1*01/DPB1*0201, and DPA1*01 and *0202/DPB1*0501. Type 2-like cells were preferentially induced in Cry j 1 stimulation, while an almost equal number of type 2-and type 1-like cells was induced in rCry j 2. Conclusions: No clear correlation existed between peptide specificity, HLA class II restriction and induction of Th-cell subsets, suggesting that the requirement of different dose of Cry j 1 or Cry j 2 to induce proliferation in PBMC may lead to distinguishable difference in induction of Th subsets between TCCs specific to Cry j 1 and Cry j 2.

L7 ANSWER 2 OF 4 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 1
1999011473 EMBASE HLA class II association with type I allergy to house dust mite and **Japanese cedar pollen** in Japanese subjects. Sadanaga Y.; Ishikawa T.; Yasueda H.; Okudaira H.; Nishimura Y.. Y. Sadanaga, Department of Otorhinolaryngology, Kumamoto University, School of Medicine, 1-1-1 Honjo, Kumamoto 860, Japan.

Ishikawa@gpo.Kumamoto-u.ac.jp. Allergology International 47/4 (285-291) 1998.
Refs: 29.
ISSN: 1323-8930. CODEN: ALINFR. Pub. Country: Australia. Language: English. Summary Language: English.

AB We evaluated the incidence of the association of HLA class II phenotype and specific IgE responsiveness against house dust mite (HDM) and/or **Japanese cedar pollen** (Jc) in 176 patients with allergic rhinitis, with or without bronchial asthma, and 107 nonallergic subjects. Specific IgE antibody titration against the purified allergens Der f1 and Der f2 from HDM, and against Cry J1 and **Cry J2** from Jc, was performed by using enzyme-linked immunosorbent assay (ELISA) and radioimmunoassay (RIA) in sera from all subjects. HLA class-II oligotyping was performed by the polymerase chain reaction sequence specific oligonucleotide (PCR-SSO) method on the DRB1*, DQA1*, DQB1* and DPB1* alleles using peripheral blood cells. The high IgE responders .gtoreq. class 4 to the purified allergens were identified by using the IgE antibody reference concentration obtained by ELISA, RIA and routine IgE CAP RAST. Compared to the controls, the patients with both rhinitis and asthma showed significantly higher frequencies of DRB1*0901, DQB1*0303, and DPB1*0401 alleles. High IgE responsiveness to HDM was associated with DRB1* 1101, 0901, DQB1*0303, and DPB1*0401 alleles. The patients with anti-Der f1 IgE antibody concentration exceeding 72.2 ng/mL showed significantly elevated frequencies for DQB1*0401 and DPB1*0401 alleles. and those with anti Der f2 IgE antibody concentration exceeding 46.2 ng/mL showed significantly elevated frequencies for DPB1*0401 and 0901 alleles. High IgE responsiveness to Jc with Cry j1 and **Cry j2** was associated with the DRB1*1201 alleles.

L7 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS

1997:88362 Document No. 126:184989 Analysis of T cell response to major allergens of Japanese ceder and cypress pollen. Yamaguchi, Hiroshi (Daisan Hosp. II, Jikei Univ. Sch. Med., Komae, 201, Japan). Tokyo Jikeikai Ika Daigaku Zasshi, 111(6), 949-956 (Japanese) 1996. CODEN: TJIDAH. ISSN: 0375-9172. Publisher: Tokyo Jikeikai Ika Daigaku Seiikai.

AB Antigen-specific CD4+ T cells play an important role in allergic sensitization by secreting lymphokines that promote IgE formation or maturation of effector cells such as eosinophils and mast cells. Murine and human T cell responses to Cry j1, **Cry j2** (major allergens of **Japanese cedar pollen**), and Cha o1 (major allergen of Japanese cypress pollen) were investigated. First, proliferative response of lymph node cells (LNC) from 3 strains (BALB/c B10, D2, and B10 mice) primed with each allergen were examd. T cells from all strains showed a strong proliferative response to Cha o1 and **Cry j2** but showed a wk or no response to Cry j1. Furthermore, each allergen-primed LNC and established Cha o1- or **Cry j2**-specific T cell line showed no cross reactivity with other pollen allergens. These results suggest that there is no common T cell epitopes recognized by these murine T cells among Japanese cedar and cypress pollen. Secondly, proliferative response of peripheral blood mononuclear cell (PBMC) from pollinosis patients to each allergen was investigated. PBMC from most of the patients strongly responded to Cry j1, **Cry j2**, and Cha o1. Interestingly, PBMC from 1 patient showed a strong response to Cha o1 and **Cry j2** but no response to Cry j1 in a similar pattern of murine T cell response. In contrast, there was no response to each allergen in healthy donors. These results clearly indicate that not only Cry j1 and **Cry j2** but also Cha o1 is a very important pollen allergen, and there is a unique T cell epitope on each pollen allergen.

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS

1995:770401 Document No. 123:253872 Cry j 2, a major allergen of **Japanese cedar pollen**, shows polymethylgalacturonase activity. Ohtsuki, T.; Taniguchi, Y.; Kohno, K.; Fukuda, S.; Usui, M.; Kurimoto, M. (Fujisaki Institute, Hayashibara

Biochemical Laboratories, Inc, Okayama, 702, Japan). Allergy (Copenhagen), Volume Date 1995, 50(6), 483-8 (English) 1995. CODEN: LLRGDY. ISSN: 0105-4538.

AB We examd. Cry j 2, a major allergen of Japanese cedar (Cryptomeria japonica) pollen, for polygalacturonase enzyme activity, since a nucleotide sequence of cDNA of Cry j 2 showed a significant homol. with that of tomato polygalacturonase. Polygalacturonase is well known to depolymerize preferentially polygalacturonic acid (PGA) by hydrolysis. However, Cry j 2 did not act on PGA, but was found to depolymerize pectin and methylesterified PGA in a dose-dependent manner. The substrate specificity of Cry j 2 was different from that of polygalacturonase derived from Aspergillus niger. The depolymg. activity of Cry j 2 reached a max. at 50%-60% of methylesterification of PGA. In contrast, polygalacturonase showed its max. activity to PGA, and the activity decreased as the degree of methylesterification increased. Interestingly, the pectin-depolymg. activity of Cry j 2 was due to a hydrolysis, but not a lyase, activity which splits the glycosidic bonds by .beta.-elimination, since no unsatd. uronides were found by measurement of absorbance at 235 nm in the reaction mixt. The enzyme activity was markedly inhibited by anti-Cry j 2 antibodies. These results indicate that Cry j 2 probably has polymethylgalacturonase enzyme activity, as postulated by von Neukom in 1963, although existence of this activity has not yet been proven.

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=> s sone t?/au or kume a?/au or dairiki k?/au or kino k?/au
L8        3213 SONE T?/AU OR KUME A?/AU OR DAIRIKI K?/AU OR KINO K?/AU

=> s l8 cedar pollen allergen
MISSING OPERATOR L8 CEDAR
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l18 and cedar pollen allergen
L18 NOT FOUND
The L-number entered could not be found.  To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l8 and cedar pollen allergen
L9            7 L8 AND CEDAR POLLEN ALLERGEN

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10           3 DUP REMOVE L9 (4 DUPLICATES REMOVED)

=> d l10 1-3 cbib abs

L10  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2002 ACS
1998:338149   Document No. 129:27001  Peptide immunotherapeutic agent.
     Sone, Toshio; Kume, Akinori; Dairiki, Kazuo;
     Kino, Kohsuke (Meiji Milk Products Co., Ltd., Japan; Sone, Toshio;
     Kume, Akinori; Dairiki, Kazuo; Kino, Kohsuke).  PCT Int. Appl. WO 9820902
     A1 19980522, 51 pp.  DESIGNATED STATES: W:  AU, CA, CN, JP, KR, US; RW:
     AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE.
     (Japanese).  CODEN: PIXXD2.  APPLICATION: WO 1997-JP4129 19971112.
     PRIORITY: JP 1996-302053 19961113.
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AB A peptide immunotherapeutic agent useful for each individual patient suffering from an allergy, and a reagent for a typing test on HLA class II mols. of the patient to be used in the selection of a peptide immunotherapeutic agent useful for each individual patient suffering from an allergy. The peptide immunotherapeutic agent permits the optimal peptide immunotherapy for each individual patient, so that a marked improvement in peptide immunotherapy can be expected. Further, it has become possible to provide a peptide immunotherapeutic agent which is useful also for patients who cannot be covered by peptide immunotherapy by a major antigen peptide recognized in a particular patient population.

Furthermore, it has also become possible to conveniently conduct typing of HLA class II mols. of patients suffering from an allergy by using the antigen peptide of the invention. Thus, T cell epitopes of Japanese **cedar pollen allergen** Cry i 1 and 2 were identified for immunotherapy of allergy.

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS
1996:248631 Document No. 124:315051 Epitopes of Japanese **cedar pollen allergen** Cry j II for therapeutics and prophylactics. **Sone, Toshio**; Komyama, Naoki; Kii, Kosuke (Meiji Milk Prod Co Ltd, Japan). Jpn. Kokai Tokkyo Koho JP 08047392 A2 19960220 Heisei, 17 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1994-297840 19941107. PRIORITY: JP 1993-276773 19931105; JP 1994-134868 19940526.
AB A cDNA sequence encoding allergen Cry j II is isolated from a cDNA library of Japanese cedar (sugi or Cryptomeria japonica) and its amino acid sequence deduced. T-cell epitopes derived from the Cry j II allergen are provided which can be used for the prevention, diagnosis, and treatment of Japanese cedar pollinosis.

L10 ANSWER 3 OF 3 MEDLINE DUPLICATE 1
96408730 Document Number: 96408730. PubMed ID: 8813737. Japanese cedar pollinosis and HLA-DP5. Hori T; Kamikawaji N; Kimura A; **Sone T**; Komiyama N; Komiyama S; Sasazuki T. (Department of Genetics, Medical Institute of Bioregulation, Kyushu University, Fukuoka, Japan.) TISSUE ANTIGENS, (1996 Jun) 47 (6) 485-91. Journal code: VSV; 0331072. ISSN: 0001-2815. Pub. country: Denmark. Language: English.
AB Japanese cedar pollinosis is a type I allergic disease caused by Japanese cedar (Cryptomeria japonica) pollen. We investigated the association between the disease and HLA class II alleles by HLA-DNA typing using a PCR-SSOP method and found that the frequency of HLA-DP5 (DPA1*02022 and DPB1*0501) was significantly increased in the patients. To investigate whether the HLA-DP5 molecule is directly involved in the pathogenesis of the disease, Japanese cedar pollen antigen (CPAg)-specific T cell lines were established from 3 patients who possessed HLA-DP5 (DPA1*02022/ DPB1*0501). By using these CPAg-specific T cell lines and HLA class II-expressing L-cell transfectants, we found that disease-associated HLA-DP5 restricted T cells specific for CPAg existed in the patients. Furthermore, among 38 synthesized overlapping peptides spanning the entire length of one of the major Japanese **cedar pollen allergens**, Cry j 1, an immunodominant peptide which induced HLA-DP5 restricted Th2 was identified. These observations suggest that the HLA-DP5 may be involved, at least in part, in the pathogenesis, by helping the IgE antibody production against CPAg.

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=> s peptide therapy
L11        383 PEPTIDE THERAPY

=> s l11 and cedar pollen
L12          0 L11 AND CEDAR POLLEN

=> s l11 and allergy
L13         23 L11 AND ALLERGY

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L23 NOT FOUND
The L-number entered could not be found.  To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l13 and cedar
L14          0 L13 AND CEDAR

=> s l13 and T cell epitope
   3 FILES SEARCHED...
L15          2 L13 AND T CELL EPITOPE
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PROCESSING COMPLETED FOR L15
L16            2 DUP REMOVE L15 (0 DUPLICATES REMOVED)

=> d l16 1-2 cbib abs

L16  ANSWER 1 OF 2  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1995:143746  Document No.: PREV199598158046. Evaluation of T
     cell epitope defined peptides from cat allergen by
     bronchial challenge. Creticos, P. S. (1); Spector, S L.; Busse, W. W.;
     Israel, E.; Nicodemus, C. F.; Jones, N. H.; Olson, T.; Gefter, M. L.;
     Lichtenstein, L. M.; Norman, P. S.. (1) Baltimore, MD USA. Journal of
     Allergy and Clinical Immunology, (1995) Vol. 95, No. 1 PART 2, pp. 390.
     Meeting Info.: Fifty-first Annual Meeting of the American Academy of
     Allergy and Immunology New York, New York, USA February 24-March 1, 1995
     ISSN: 0091-6749. Language: English.

L16  ANSWER 2 OF 2  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1995:143747  Document No.: PREV199598158047. Initial clinical experience with
     T cell epitope defined peptides from ragweed
     allergen Amb a 1. Lichtenstein, L. M. (1); Creticos, P. S.; Norman, P. S.;
     Jones, N. H.; Settles, M.; Wallner, B.; Nicodemus, C. F.. (1) Baltimore,
     MD USA. Journal of Allergy and Clinical Immunology, (1995) Vol. 95, No. 1
     PART 2, pp. 390. Meeting Info.: Fifty-first Annual Meeting of the American
     Academy of Allergy and Immunology New York, New York, USA February
     24-March 1, 1995 ISSN: 0091-6749. Language: English.


=> d his

     (FILE 'HOME' ENTERED AT 13:50:23 ON 02 MAR 2002)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 13:50:41 ON
     02 MAR 2002
L1             0 S JANPANESE CEDAR POLLEN
L2           707 S JAPANESE CEDAR POLLEN
L3           113 S L2 AND "CRY J 1"
L4            35 S L3 AND T CELL EPITOPE
L5            12 DUP REMOVE L4 (23 DUPLICATES REMOVED)
L6             5 S L2 AND "CRY J2"
L7             4 DUP REMOVE L6 (1 DUPLICATE REMOVED)
L8          3213 S SONE T?/AU OR KUME A?/AU OR DAIRIKI K?/AU OR KINO K?/AU
L9             7 S L8 AND CEDAR POLLEN ALLERGEN
L10            3 DUP REMOVE L9 (4 DUPLICATES REMOVED)
L11          383 S PEPTIDE THERAPY
L12            0 S L11 AND CEDAR POLLEN
L13           23 S L11 AND ALLERGY
L14            0 S L13 AND CEDAR
L15            2 S L13 AND T CELL EPITOPE
L16            2 DUP REMOVE L15 (0 DUPLICATES REMOVED)

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PROCESSING COMPLETED FOR L13
L17           18 DUP REMOVE L13 (5 DUPLICATES REMOVED)

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MISSING OPERATOR L17 1-18
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> d l17 1-18 cbib abs

L17  ANSWER 1 OF 18     MEDLINE                          DUPLICATE 1
2002003224  Document Number: 21623299.    PubMed ID: 11750046.   Anti-allergen
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antibodies can be neutralized by antibodies obtained against a peptide complementary to the allergen: towards a new **peptide therapy** for **allergy**. Selo Isabelle; Creminon Christophe; Grassi Jacques; Couraud Jean Yves. (CEA, Service de Pharmacologie et d'Immunologie, DSV/DRM Ctr d'Etudes de Saclay, Bat. 136, CE Saclay, 91191, Cedex, Gif-sur-Yvette, France.) IMMUNOLOGY LETTERS, (2002 Feb 1) 80 (2) 133-8. Journal code: 7910006. ISSN: 0165-2478. Pub. country: Netherlands. Language: English.

AB The concept of specific immune treatment against allergic diseases requires the development of antibodies capable of specifically neutralizing anti-allergen antibodies. The aim of the present study was to investigate whether a novel approach, consisting in raising anti-idiotypic blocking antibodies through peptide immunization, could be envisaged in the field of **allergy**. Using **allergy** to cow's milk as a model, we prepared polyclonal antibodies against a peptide that is complementary (i.e. hydropathically opposed) to a major epitope of bovine beta-lactoglobulin (BLG), one of the main allergens of bovine milk. Anti-complementary peptide antibodies were found to neutralize in vitro both well-characterized anti-BLG monoclonal antibodies from mice sensitized to BLG and anti-BLG IgE from two patients suffering from milk **allergy**. These results suggest a new strategy for the functional inhibition of specific disease-associated IgE that may be applicable to the specific treatment of various allergic disorders.

L17 ANSWER 2 OF 18 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

2002018179 EMBASE [Specific immunotherapy in allergic rhinoconjunctivitis: Current standard and new approaches]. SPEZIFISCHE IMMUNTHERAPIE (HYPOSENSIBILISIERUNG) BEI ALLERGISCHER RHINO-KONJUNKTIVITIS - BEWAHRTES UND NEUES. Klimek L.; Renz H.. Dr. L. Klimek, HNO, Allergologie, Umweltmedizin, An den Quellen 10, D-65183 Wiesbaden, Germany. Allergologie 24/12 (569-579) 2001.
Refs: 58.
ISSN: 0344-5062. CODEN: ALLRDI. Pub. Country: Germany. Language: German. Summary Language: English; German.

AB Specific immunotherapy (SIT) of allergic disorders as introduced by Freeman and Noon involves application of gradually increasing doses of extracts of the material to which the individual is sensitive. SIT represents the only specific treatment that can be offered to allergic patients besides allergen avoidance. SIT has been widely used in pollen allergic rhinitis, and the clinical efficacy has been demonstrated in several controlled clinical trials. The underlying mechanism of this treatment is still not understood. Previous studies have focussed on changes in serum antibodies, including blunting of seasonal rises in specific IgE and increase in specific IgG antibodies, especially of the IgG4 isotype. Recent studies suggested an effect on T lymphocytes, leading to a switch from a predominant Th2 response (IL-4, IL-5) to a Th1 response (IFN-.gamma.). The switch of cytokine profile to a predominant IFN-.gamma. response results in inhibition of IL-4 dependent IgE production, reinforced by a decrease in the production of IL-4 by Th2 cells. SIT was shown to be an effective treatment modality in allergic rhinoconjunctivitis. It decreased symptoms, medication intake, reactivity in specific nasal and conjunctival provocation tests, inflammatory markers and might induce a switch from a predomination Th2 cell profile to a Th1 profile. Efficacy of SIT is dependend on the allergen the individual patient is sensitive to, the quality and total amount of allergen applied, and the SIT schedule. New therapeutic options include **peptide-therapy**, genetherapeutic immunotherapy, anti-T-Cell therapy and modification of cytokine-production.

L17 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2002 ACS

2000:244696 Document No. 133:57193 Immunotherapy for food **allergies** : past, present, future. Lehrer, Samuel B.; Wild, Laurianne G.; Bost, Kenneth L.; Sorensen, Ricardo U. (Division of Allergy and Clinical Immunology, Department of Medicine, Tulane University Medical Center, New Orleans, LA, USA). Clin. Rev. Allergy Immunol., 17(3), 361-381 (English)

1999. CODEN: CRAIF2. ISSN: 1080-0549. Publisher: Humana Press Inc..
AB A review with 65 refs. An overview of the gut mucosal immune response, along with the traditional and novel approaches to immunotherapy such as immune complex therapy, **peptide therapy**, anti-IgE and DNA immunization are discussed. A discussion of mucosal vaccines and advances in the development of hypo-allergenic foods through biotechnol. to reduce IgE binding capacity of the allergenic proteins is also presented.

L17 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2002 ACS
2000:53735 Document No. 133:15980 Tolerogenic peptides: Clinical experience in **allergy**. Nicodemus, Christopher F.; Philip, George (Diatide, Inc., Londonderry, NH, USA). Lung Biol. Health Dis., 136(Immunotherapy in Asthma), 327-336 (English) 1999. CODEN: LBHDD7. ISSN: 0362-3181. Publisher: Marcel Dekker, Inc..
AB A review with 28 refs. The T cell component of antigen-specific immune response has been targeted for therapeutic strategies to modify diseases characterized by dysregulated immune response. This review focuses on scientific rationale and early clin. experience in **allergy**. T cell provide stimulatory signal for B cell proliferation and antigen prodn. after the B cells bind antigen by the specific antibody expressed on B cell surface and sol. peptide fragments in high doses can render T cell nonresponsive and the mechanism of this anergy is discussed. Experience from perennial and seasonal **allergies**, anaphylactic syndromes and the safety of **peptide therapy** are also reviewed.

L17 ANSWER 5 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1998:257468 Document No.: PREV199800257468. Effects of **peptide therapy** on ex vivo T-cell responses. Marcotte, Gregory V.; Braun, Christine M.; Norman, Philip S.; Nicodemus, Christopher E.; Kagey-Sobotka, Anne; Lichtenstein, Lawrence M.; Essayan, David M. (1). (1) Johns Hopkins Asthma Allergy Center, 5501 Hopkins Bayview Circle, Baltimore, MD 21224 USA. Journal of Allergy and Clinical Immunology, (April, 1998) Vol. 10, No. 4 PART 1, pp. 506-513. ISSN: 0091-6749. Language: English.
AB Background: **Peptide therapy** targets T cells directly with short peptides containing multiple T-cell receptor epitopes. Murine studies suggest T-cell anergy as the mechanism of action; however, changes in T-cell cytokine profiles may be more relevant in human beings. Objective: We sought to study the effects of **peptide therapy** on ex vivo antigen-specific T-cell responses. Methods: Antigen-specific T-cell lines were generated from subjects enrolled in a double-blind, placebo controlled, two-dose study of the ALLERVAX CAT therapeutic, containing Fel d 1 peptides (ImmuLogic Pharmaceutical Corp., Waltham, Mass.) (n=7, 8, and 7, respectively, for groups receiving placebo, 75 mug, or 750 mug). Each subject had three lines propagated before and after receiving **peptide therapy**; antigens used were cat hair extract, Fel d 1 peptides, and tetanus toxoid (negative control). Proliferative responses and cytokine generation from each line were assessed after two restimulations with antigen and autologous antigen-presenting cells. Results: The Fel d 1 peptide lines showed a dose-dependent decrease of IL-4 production ($p=0.02$ and 0.025, respectively, for the 750 Kg group vs both the 75 mug and placebo groups). IL-4 production from the cat hair allergen extract lines and interferon-gamma production from both the Fel d 1 peptide lines and cat hair allergen extract lines showed no statistically significant changes. The control tetanus toxoid lines showed no changes in cytokine production; there were no significant changes in proliferation with any of the antigens in any of the treatment groups. In the clinical arm of the trial, only the 750 mug dose of peptides produced a significant response. Conclusions: **Peptide therapy** induces a significant, dose-dependent decrease in peptide-stimulated IL-4 production, consistent with either a shift in T-cell phenotype or peptide-specific T-cell tolerance.

L17 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2002 ACS
1998:280991 Document No. 129:103924 Effects of **peptide therapy** on ex vivo T-cell responses. Marcotte, Gregory V.; Braun, Christine M.; Norman, Philip S.; Nicodemus, Christopher F.; Kagey-Sobotka, Anne; Lichtenstein, Lawrence M.; Essayan, David M. (The Division of Clinical Immunology, Johns Hopkins University School of Medicine, Baltimore, MD, USA). J. Allergy Clin. Immunol., 101(4, Pt. 1), 506-513 (English) 1998. CODEN: JACIBY. ISSN: 0091-6749. Publisher: Mosby, Inc..
AB **Peptide therapy** targets T cells directly with short peptides contg. multiple T-cell receptor epitopes. Murine studies suggest T-cell anergy as the mechanism of action; however, changes in T-cell cytokine profiles may be more relevant in human beings. We sought to study the effects of **peptide therapy** on ex vivo antigen-specific T-cell responses. Antigen-specific T-cell lines were generated from subjects enrolled in a double-blind, placebo controlled, two-dose study of the ALLERVAX CAT therapeutic, contg. Fel d 1 peptides (ImmuLogic Pharmaceutical Corp., Waltham, Mass.) (n = 7,8, and 7, resp., for groups receiving placebo, 75 .mu.g, or 750 .mu.g). Each subject had three lines propagated before and after receiving **peptide therapy**; antigens used were cat hair ext., Fel d 1 peptides, and tetanus toxoid (neg. control). Proliferative responses and cytokine generation from each line were assessed after two re-stimulations with antigen and autologous antigen-presenting cells. The Fel d 1 peptide lines showed a dose-dependent decrease of IL-4 prodn. (p = 0.02 and 0.025, resp., for the 750 .mu.g group vs both the 75 .mu.g and placebo groups). IL-4 prodn. from the cat hair allergen ext. lines and interferon-.gamma. prodn. from both the Fel d 1 peptide lines and cat hair allergen ext. lines showed no statistically significant changes. The control tetanus toxoid lines showed no changes in cytokine prodn.; there were no significant changes in proliferation with any of the antigens in any of the treatment groups. In the clin. arm of the trial, only the 750 .mu.g dose of peptides produced a significant response. **Peptide therapy** induces a significant, dose-dependent decrease in peptide-stimulated IL-4 prodn., consistent with either a shift in T-cell phenotype or peptide-specific T-cell tolerance.

L17 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2002 ACS
1998:389488 Document No. 129:39843 The recent aspects on treatment and management of allergic disease. The mechanism and management of bronchial asthma. Kokubu, Fumio; Adachi, Mitsuru (Sch. Med., Showa Univ., Tokyo, 142, Japan). Showa Igakkai Zasshi, 58(1), 1-8 (Japanese) 1998. CODEN: SIGZAL. ISSN: 0037-4342. Publisher: Showa Daigaku, Showa Igakkai.
AB A review with 19 refs., on the pathogenesis, pathophysiol., and treatment of allergic diseases, discussing genetic factors, chemokines in allergic inflammation, treatment of bronchial asthma, **peptide therapy**, and airway monitoring in the treatment of asthma.

L17 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2002 ACS
1997:195702 Document No. 126:190921 Preparations and methods for the treatment of T cell-mediated diseases. Cohen, Irun R.; Elias, Dana; Shinitzky, Meir (Yeda Research and Development Co. Ltd., Israel; Cohen, Irun R.; Elias, Dana; Shinitzky, Meir). PCT Int. Appl. WO 9702016 A1 19970123, 38 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US11373 19960702. PRIORITY: IL 1995-114458 19950705.
AB Metabolizable lipid emulsions, such as Intralipid and Lipofundin, are excellent vehicles for **peptide therapy** of autoimmune diseases and of other TH1 T cell-mediated diseases or conditions, as it promotes TH1 to TH2 cytokine shift. Such emulsions may be used in conjunction with an antigen recognized by inflammatory T cells assocd. with the pathogenesis of a T cell-mediated disease or condition for the

therapeutic treatment of such a condition.

L17 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2002 ACS
1997:597644 Document No. 127:229122 New ideas in the treatment of asthma. Arai, Motonaka; Nakagawa, Takemasa (Toyoko Byoin, Sei Marianna Ika Daigaku, Kawasaki, 211, Japan). Ensho to Men'eki, 5(5), 556-564 (Japanese) 1997. CODEN: ENMEFA. ISSN: 0918-8371. Publisher: Sentan Igakusha.
AB A review with 23 refs., on present state of treatment and management of bronchial asthma using .beta.2-agonists, theophylline, steroids, and **allergy** inhibitors. Possible application of immunosuppressants, cytokine antagonists, IgE-binding inhibitors, and **peptide therapy** are also discussed.

L17 ANSWER 10 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1996:145433 Document No.: PREV199698717568. The cat room model for associating allergen levels with asthma symptoms and evaluating treatment effects of **peptide therapy**. Ohman, J. L. (1); Bennett, D. V.; Happ, M. P.; Settles, M. R.; Jones, N. H.; Hirani, S.; Long, A. A.. (1) Boston, MA USA. Journal of Allergy and Clinical Immunology, (1996) Vol. 97, No. 1 PART 3, pp. 387. Meeting Info.: Fifty-second Annual Meeting of the American Academy of Allergy Asthma and Immunology New Orleans, Louisiana, USA March 15-20, 1996 ISSN: 0091-6749. Language: English.

L17 ANSWER 11 OF 18 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 2
96225063 EMBASE Document No.: 1996225063. **Peptide therapy** for treatment of allergic diseases. Wallner B.P.; Gefter M.L.. ImmuLogic Pharmaceutical Corporation, 610 Lincoln Street,Walthan, MA 02154, United States. Clinical Immunology and Immunopathology 80/2 (105-109) 1996. ISSN: 0090-1229. CODEN: CLIIAT. Pub. Country: United States. Language: English.

L17 ANSWER 12 OF 18 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
96044885 EMBASE Document No.: 1996044885. Peptide modulation of allergen-specific immune responses. Hoyne G.F.; Kristensen N.M.; Yssel H.; Lamb J.R.. Infection and Immunity Section, Department of Biology, Imp Coll Science Technology Medicine, Prince Consort Road,London SW7 2BB, United Kingdom. Current Opinion in Immunology 7/6 (757-761) 1995. ISSN: 0952-7915. CODEN: COPIEL. Pub. Country: United Kingdom. Language: English. Summary Language: English.
AB In vitro peptide stimulation of allergen-reactive T-helper type 1 and type 0 cells, in the absence of costimulatory signals, induces anergy that is accompanied by the modulation of cell surface phenotype and changes in cytokine production. In experimental animal models, the administration of allergen-derived peptides may result in the downregulation of cytokine and antibody production, which is preceded by transient activation of CD4+ T cells, without the induction of effector immunity. Preliminary results of clinical trials using allergen-derived peptides for desensitization are becoming available and should provide some insight into the efficacy of **peptide therapy** in man.

L17 ANSWER 13 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1995:143746 Document No.: PREV199598158046. Evaluation of T cell epitope defined peptides from cat allergen by bronchial challenge. Creticos, P. S. (1); Spector, S L.; Busse, W. W.; Israel, E.; Nicodemus, C. F.; Jones, N. H.; Olson, T.; Gefter, M. L.; Lichtenstein, L. M.; Norman, P. S.. (1) Baltimore, MD USA. Journal of Allergy and Clinical Immunology, (1995) Vol. 95, No. 1 PART 2, pp. 390. Meeting Info.: Fifty-first Annual Meeting of the American Academy of Allergy and Immunology New York, New York, USA February 24-March 1, 1995 ISSN: 0091-6749. Language: English.

L17 ANSWER 14 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
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AB A review with 8 refs. on IgE-mast cell pathway and T cell-eosinophil pathway in type I allergic reactions, mechanisms of antigen recognition by T cells, mechanisms of T cell activation, induction of T cell anergy, and clin. applications of T cell anergy.

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1994:150295 Document No.: PREV199497163295. Immune mechanism of house dust mite induced allergic disorder in mice. Buck, J. (1); Cheng, K. C. (1); Zhang, Y. (1); Watanabe, T. (1); Krug, M. (1); Chang, H. K. (1); Park, S. J.; Yoo, T. J. (1). (1) Memphis, TN USA. Journal of Allergy and Clinical Immunology, (1994) Vol. 93, No. 1 PART 2, pp. 192. Meeting Info.: Fiftieth Annual Meeting of the American Academy of Allergy and Immunology Anaheim, California, USA March 4-9, 1994 ISSN: 0091-6749. Language: English.

L17 ANSWER 18 OF 18 SCISEARCH COPYRIGHT 2002 ISI (R)
93:629690 The Genuine Article (R) Number: MB332. IMMUNOTHERAPY OF ALLERGIC DISEASES. NAKAGAWA T (Reprint); GERSHWIN M E. ST MARIANNA MED UNIV, SCH MED, INST MED SCI, 2-16-1 SUGAE, MIYAMAE KU, KAWASAKI 216, JAPAN (Reprint); UNIV CALIF DAVIS, DIV RHEUMATOL ALLERGY & CLIN IMMUNOL, DAVIS, CA, 95616. INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY (1993) Vol. 102, No. 2, pp. 117-120. ISSN: 1018-2438. Pub. country: JAPAN; USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Immunotherapy (IT) of IgE-mediated diseases has been used since its first description in 1911. This therapy has been used in patients with inhalant **allergy** and insect venom sensitivity. Unfortunately. IT suffers from the crudeness of the **allergy** extracts and the inability to define allergenic epitopes. Moreover, this form of IT has been increasingly questioned because of improvements in pharmacotherapy and the risks of untoward reactions. These untoward reactions even include anaphylaxis and death. Despite this criticism, there are increasing data on the efficacy of immunotherapy and considerable research is underway to improve the risk-benefit ratio of treatment. Other approaches directed at inhibiting the sequential events of both the afferent and efferent limbs of allergic reactions are in progress. This involves specific alterations of target cells, i.e., mast cells and basophils. Moreover, the development of recombinant allergens and the precise definition of the binding site of IgE will further promote research and development of new means of IT. Gene targeting therapy may follow, directed at T cells specific for allergen epitope(s) or IgE binding sites. The future holds great promise and excitement.

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